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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SGAGIAS, MAGDALENE K	
ART UNIT	PAPER NUMBER
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/646,970	PHELPS, CAROL J.	
	Examiner	Art Unit	
	Magdalene K. Sgagias	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21 and 40-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21 and 40-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/03/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-21, 40-50 are pending and under consideration. Claims 22-39 are cancelled.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-16 and 40-50, in the reply filed on 12/4/06 are acknowledged.

Claims 1-16, 40-50 are directed to a product. Pursuant to the procedures set forth in MPEP § 821.04(B), claims 17-21, are directed to the process of making or using a product, previously withdrawn from consideration as a result of a restriction requirement, claims 17-21 hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Because all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, **the restriction requirement as set forth in the Office action mailed on 6/1/06 is hereby withdrawn**. In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the

provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claims 1-21, 40-50 are under consideration.

Claim Objections

Claim 43, 48 is objected to because of the following informalities: Claim depends from the cancelled claim 22. Appropriate correction is required.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.
In addition, the specification contains inappropriate characters as letters throughout the document. For example, see page 55, line 26, wherein a square character denotes a measurement unit, also see page 6 for embedded hyperlink.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims **1-16, 40-46** are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are directed to an animal including a pig that lacks any expression of functional alpha 1,3

galactosyltrasferase. However, the scope of the claims can be interpreted to include a pig that contains a naturally occurring lack of expression of functional alpha 1,3 galactosyltrasferase. The tissues and cells of claims 8-16 are included in this rejection since they are not isolated and read on tissues and cells in vivo. As such, the claims read on a product of nature, which is non-statutory subject matter.

Claims **43-46,** are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims require providing an animal, the scope of which encompasses a human. Humans are considered non-statutory subject matter. See 1077 O.G. 24, April 21, 1987

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims **8, 13, 40, 42, 47-50** are rejected under 35 U.S.C. 102(b) as being anticipated by **Gustafsson et al,** (6,153,428; Nov 28, 2000).

Gustafsson et al, teaches a tissue of a pig that lacks expression of functional a(1,3) galactosyltransferase (abstract) (claim **8**).

Gustafsson et al, teaches a porcine cell which is interpreted to read on tissue that lacks any expression of functional α(1,3) galactosyltransferase (column 6, lines 2-9) (claims **8** and **13**).

Gustafsson et al, teaches a porcine cell that carries a homozygous knock out for the gal alpha-1,3-GT gene (column 6, lines 1-9 and column 7, lines 1-10)) (claim **40**).

Gustafsson et al, teaches a porcine cell that carries a homozygous knock out for the gal alpha-1,3-GT gene in which at least one allele contains an induced mutation in the α(1,3) galactosyltransferase gene (column 6, lines 40-42) (claim **42**).

The cells of claims 47-50 are the same as those of Gustafsson since the only requirement is knock out alpha-1,3-GT gene in which at least one allele contains an induced mutation in the α(1,3) galactosyltransferase gene (column 6, lines 40-42); column 6, lines 2-9), (claims **47-50**).

Claims **1-16, 40, 42-44, 46-49** are rejected under 35 U.S.C. 102(e) as being anticipated by **Denning et al,** (US 7,126,039 B2, Date of Patent: Oct. 24, 2006; Filed: Mar. 21, 2002).

Denning et al, teaches a pig that lacks expression of alpha.1,3 GT gene, (see claim 1, and column 99, lines 26-27), (claim **1**)

Denning et al, teaches and organ of a pig that lacks expression of functional of alpha,1,3 GT gene, wherein the organ is kidney, liver, heart, lung, pancreas, (column 22, lines 53-61) (claims **2-7**).

Denning et al, teaches a tissue of a pig that lacks expression of functional alpha,1,3 GT gene, wherein the tissue is any type of tissue such as solid tissue, cartilage (column 22, lines 58-59) (claims **8-12**).

Denning et al, teaches a cell from a pig a pig that lacks expression of functional of alpha,1,3 GT gene, wherein the cell is derived from the pancreas, Langerhans cell or insulin secreting cell (column 22, lines 59-61) (claims **13-16**).

Denning teaches a cell that carries a homozygous knock out for the alpha,1,3 GT gene, wherein at least one allele contains an induced mutation in the alpha,1,3 GT gene (see claim 1, and column 99, lines 26-27, column 23, lines 5-16) (claims **40, 42**).

Denning et al, teaches an animal produced by nuclear transfer cloning using the cell which carries a homozygous knock out for the alpha,1,3 GT gene, as a nuclear donor by nuclear transfer cloning technology (see claim 1, column 99, lines 26-27), (claims **43-44, 46**).

Denning et al, teaches cells from the animal that lacks expression of functional of alpha,1,3 GT gene, for use as an in vivo or ex vivo supplement or replacement for recipient cells (column 23, lines 5-19) (claim **47**).

Denning et al, teaches cells from the animal produced by nuclear transfer technology, wherein cells can be used for an in vivo or ex vivo supplement or replacement for recipient cells (column 23, lines 5-19) (claims **48-49**). As such Denning et al, anticipates claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims **17-21, 43-50** are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the production of a pig that lacks expression of functional α(1,3) galactosyltransferase comprising breeding a male pig heterozygous for the α(1,3) galactosyltransferase gene with a female pig heterozygous for the α(1,3) galactosyltransferase gene, wherein pigs are heterozygous due to the presence of a T-to G point mutation in an allele at the second base of exon 9 of the α(1,3) galactosyltransferase gene, or producing said pig by nuclear transfer technology, does not reasonably provide enablement for methods of producing pigs by embryonic stem cell technology or producing animals by nuclear transfer technology other than said pig. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims **17-21**, are directed to method of producing a pig that lacks expression of functional α(1,3) galactosyltransferase gene by breeding a male pig heterozygous for the α(1,3) galactosyltransferase gene with a female pig heterozygous for the α(1,3) galactosyltransferase gene. Embodiments limit the mutation to a T-to G point mutation at the second base of exon 9 of the α(1,3) galactosyltransferase gene.

Claims **17-21** embrace a pig produced by embryonic cell (ES) knock out technology. However, it is well known in the knockout art that production of knockout non-human animals other than mice is undeveloped. This is because ES cell technology is presently limited to the mouse system as only mouse ES cells achieve germline transmission of a disrupted target gene (**Hochepied et al,** Stem Cells, 22: 441-447, 2004) (abstract). Given the undeveloped and unpredictable nature of ES cells it would have required undue experimentation for the skilled artisan to use embryonic stem cells other than mouse without a reasonable expectation for success.

Claims **43-50** are directed to an animal and its cells and tissues and organs produced by nuclear transfer cloning using a cell that carries a homozygous knockout for the gal alpha-1,3, GT gene in which at least one allele contains a natural or spontaneous mutation in the gal alpha-1,3-GT gene, by nuclear transfer cloning using a cell produced by the method comprising: (a) exposing a population of cells to C. difficile toxin A; (b) removing cells which are adversely affected by toxin A die to the receptor-mediated cytotoxicity of the toxin; and (c) expanding and maintaining a cell that does not show the effects of receptor-mediated cytotoxicity as a nuclear donor.

The specification teaches the production of a pig by nuclear transfer cloning by the production of porcine cells heterozygous for the alpha-l,3-GT gene (example 1); the production of porcine cells homozygous for the alpha-l,3-GT gene (example 2); the selection with C.difficile Toxin A for porcine cells homozygous for the alpha-l,3-GT gene (example 3); and the generation of cloned pigs using homozygous alpha 1,3 GT-Deficient fetal fibroblasts as nuclear donors (example 4). However, the specification

has failed to teach the production of any other cloned animal other than said pig by nuclear transfer cloning using a cell that carries a homozygous knockout for the gal alpha-1,3, GT gene in which at least one allele contains a natural or spontaneous mutation in the gal alpha-1,3-GT gene, by nuclear transfer cloning using a cell produced by the method comprising: (a) exposing a population of cells to C. difficile toxin A; (b) removing cells which are adversely affected by toxin A die to the receptor-mediated cytotoxicity of the toxin; and (c) expanding and maintaining a cell that does not show the effects of receptor-mediated cytotoxicity. This technology was shown by the art to be unpredictable at the time of filing. The art teaches that the efficiency of somatic cell nuclear transfer, when measured as development to term as a proportion of oocytes used, has been very low (1-2%) (**Popejaeva et al,** Nature, 407: 86-90, 2000). **Popejaeva et al,** discusses that a variety of factors contribute to this inefficiency such as laboratory to laboratory variations, oocyte source and quality, methods of embryo culture, donor cell type, possible loss of somatic imprinting in the nuclei of the reconstructed embryo, failure to reprogram the transplanted nucleus adequate, and finally the failure of artificial methods of activation to emulate reproducibly those crucial membrane-mediated events that accompany fertilization (p 86, 2nd column, 2nd paragraph). **Oback et al**, (Cloning and Stem Cells, 4(2): 169-174, 2002) concludes that mammalian cloning is still very inefficient and requires systemic standardization and optimization of all the various steps of the procedure (p 172, 2nd column, last paragraph). The first step in nuclear cloning and a major source of experimental variation is the choice of a nuclear donor and this step is not rigorously controlled and

consequently, no cloning study to date has conclusively compared cloning efficiencies with molecularly defined donor cells types and cell cycle stages (Oback, p 172, 2nd column, last paragraph). At the time of filing, the skilled artisan would have regarded the production of a cloning animal by nuclear transfer cloning using a cell that carries a homozygous knockout for the gal alpha-1,3, GT gene in which at least one allele contains a natural or spontaneous mutation in the gal alpha-1,3-GT gene, by nuclear transfer cloning using a cell produced by the method comprising: (a) exposing a population of cells to C. difficile toxin A; (b) removing cells which are adversely affected by toxin A die to the receptor-mediated cytotoxicity of the toxin; and (c) expanding and maintaining a cell that does not show the effects of receptor-mediated cytotoxicity a being unpredictable requiring an undue amount of experimentation without a reasonable expectation of success.

Shi et al, (Differentiation, 671(2): 91-113, 2003) notes somatic cloning is an inefficient and unpredictable process, and a plethora of anomalies have been described in cloned embryos, fetuses and offsprings due to incomplete or inappropriate epigenetic reprogramming of donor nuclei is likely to be the primary cause of failures in nuclear transfer from different species (abstract). **Dinnyes et al,** (Cloning and Stem Cells, 4(1): 81-90, 2002) notes that there are several species where attempts to somatic cell cloning have been unsuccessful and the reasons for this lack of success varies between species (p 82, 2nd column 2nd paragraph). **Dinnyes et al,** further notes the effect of genetic background on nuclear transfer, wherein further studies are needed to identify which genetic combinations of donor cells and recipient cytoplasts are the most

successful and whether the extent of the problem is similar in all species (p 82, 2nd column, last paragraph bridge p 83, 1st column, 1st paragraph). Thus, given the art recognized unpredictability of producing cloned animals by nuclear transfer using a cell that carries a homozygous knockout for the gal alpha-1,3, GT gene in which at least one allele contains a natural or spontaneous mutation in the gal alpha-1,3-GT gene, especially one by the method comprising: (a) exposing a population of cells to C. difficile toxin A; (b) removing cells which are adversely affected by toxin A die to the receptor-mediated cytotoxicity of the toxin; and (c) expanding and maintaining a cell that does not show the effects of receptor-mediated cytotoxicity, these claims would not have been regarded as enabled by the skilled artisan at the time of filing.

Therefore, in view of the quantity of experimentation necessary to determine the parameters listed above for the cloning of an animal by nuclear transfer other than pig, the lack of direction or guidance provided by the specification for the cloning of an animal by nuclear transfer other than pig, the absence of working examples that correlate to the production of a cloned animal other than pig, the unpredictable state of the art with respect to production of cloned animals other than pig, and the breadth of the claims directed to all cloned animals, it would have required undue experimentation for one skilled in the art to make and/or use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 47 recites the limitation "animal" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 47 depends from claim 42 which is directed to a cell.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Magdalene K. Sgagias whose telephone number is (571) 272-3305. The examiner can normally be reached on Monday through Friday from 9:00 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, Jr., can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

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